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An Outbreak of Congenital Rubella

LORING G. DALES, MD, *and* JAMES CHIN, MD, *Berkeley, California*

A large outbreak of rubella occurred in the San Francisco Bay Area in early 1979. Later that year and in early 1980, 13 cases of confirmed or probable congenital rubella syndrome were reported. Results of a subsequent investigation strongly suggest that these two events were related in a causal manner and do not represent an indirect association based on changes in diagnostic or reporting thoroughness. To prevent such episodes in the future, renewed emphasis must be placed on routine immunization of young children of both sexes, rigorous enforcement of school-entry immunization laws and selective immunization of women of childbearing age.

A LARGE OUTBREAK of rubella occurred in the San Francisco Bay Area counties between February and May of 1979; more than 1,000 cases were reported and serological confirmation was obtained for many. Disease activity was most evident in the cities of San Jose and San Francisco. In 45 percent of reported cases, patients were of high school age or slightly older (15 to 19 years), in 23 percent they were in elementary or intermediate schools, in 17 percent they were adults (20 to 29 years) and in 15 percent they were preschoolers or older adults.

The California Department of Health Services (DHS) was notified of two therapeutic abortions done in May 1979 in pregnant women in whom rubella had developed during the outbreak; in both instances rubella virus was isolated from fetal tissue. Several cases of congenital rubella syndrome (CRS) were reported from the San Francisco Bay Area the following fall and winter. DHS records were reviewed to determine whether the rubella outbreak in the preceding winter and spring had been followed by a real increase in CRS cases.

From the Infectious Disease Section, California Department of Health Services, Berkeley.

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Reprint requests to: Loring G. Dales, MD, Infectious Disease Section, California Department of Health Services, 2151 Berkeley Way, Berkeley, CA 94704.

Methods

Reporting of rubella cases, including cases of CRS, to health departments is a legal requirement in California. DHS records were reviewed to determine the number of rubella cases reported for the calendar years 1976 through 1979 and the number of reported CRS cases born in the July-June, or *fiscal,* years 1976-1977 through 1979-1980. The July-June interval was chosen for CRS cases because rubella activity generally peaks in the late winter and spring, so that resultant CRS cases would be expected to cluster in the following fall and winter, thus overlapping two calendar years. As a means of identifying laboratory-confirmed cases of CRS that were not reported, records of rubella virus isolations made by the DHS Viral and Rickettsial Disease Laboratory in the years 1976 through 1980 were reviewed. The state laboratory was the only laboratory in Northern California carrying out diagnostic rubella virus isolations during this time. Neither the state laboratory nor any other Northern California laboratory routinely offered diagnostic rubella IgM antibody determinations before 1979. Therefore, laboratory records of rubella IgM antibody determinations were not used as a screening device in order to avoid a

ABBREVIATIONS USED IN TEXT

CRS=congenital rubella syndrome
DHS=Department of Health Services
HI=hemagglutination inhibition (titer)

secular bias in case ascertainment. A third method of searching for unreported cases, screening the state laboratory records for infants who at three months of age or older had rubella hemagglutination-inhibition (HI) titers above and beyond those expected from passive transfer of maternal antibody, was tried and abandoned because it was found to be unproductive. CRS cases discovered were classified as to diagnostic certainty in accordance with the criteria recently published by the Centers for Disease Control.[1]

Results

Reported rubella cases for the calendar years 1976 through 1979 for the five San Francisco Bay Area counties most prominently affected in the 1979 outbreak (Santa Clara, San Mateo, San Francisco, Contra Costa and Alameda) and for the remainder of the state are shown in Figure 1. As can be seen, in the five affected Bay Area counties the number of cases reported in 1979 was approximately six times higher than the numbers reported in each of the three preceding years. For the remainder of the state, no increase was seen in 1979 compared with the three previous years.

Figure 2 shows the number of confirmed or probable CRS cases discovered for the five Bay Area counties and for the rest of the state. Cases are grouped by July-June years, beginning with July 1976. According to the Centers for Disease Control criteria used, a confirmed case is one with defects consistent with CRS and one or both of the following: rubella virus isolated or rubella-specific IgM present. A probable CRS case is one with laboratory data insufficient for confirmation but with any two conditions listed under part 1, or one from part 1 and one from part 2, as follows: (1) cataracts or congenital glaucoma, congenital heart disease, loss of hearing or pigmentary retinopathy and (2) purpura or thrombocytopenia, splenomegaly, onset of jaundice within 24 hours after birth, microcephaly, mental retardation, meningoencephalitis or radiolucent bone disease.

As can be seen, there was a sharp increase in cases of CRS from the San Francisco Bay Area counties for the 1979-1980 year. Of these 13 cases, 11 were in the confirmed category (Table 1), and all 13 infants were born between July 1979 and February 1980, which fits well temporally with the prior rubella outbreak in the late winter of 1978 and spring of 1979. For 11 of the infants, the mothers' ages at delivery were available. The range was 17 to 34 years (mean of 21.4 years). In 70 percent of the women, a history of rash illness or exposure to rash illness during pregnancy existed. Information was not available on the sources of exposure for these women, on whether these rash illnesses or exposures to rash illness were reported to the medical staff providing their prenatal care, and on whether therapeutic abortions were considered. Also, information on the total number of therapeutic abortions done as a result of the 1979 outbreak was not available, although—as mentioned earlier—two such events were reported to the DHS.

In addition to the confirmed and probable cases presented in Figure 2, during the 1979-1980 year four cases of possible CRS (compatible clinical findings that did not quite meet the criteria for a probable case) and four cases of infection only (laboratory evidence of congenital rubella infection without apparent defects) were reported from the San Francisco Bay Area counties. These additional cases represented increases over the corresponding counts for the rest of the state and for the San Francisco Bay Area counties in the preceding three years.

Discussion

While rubella is a reportable disease in California, most cases of this usually mild illness are not reported; many are not even clinically recognized. Nonetheless, the data on reported cases shown in Figure 1 reflect the 1979 rubella outbreak in the San Francisco Bay Area. An increment in rubella cases reported from the rest of the state is noted for 1977, but this is suspected to be largely artifact, reflecting diagnoses made during a large measles outbreak that erupted in Southern California early that year.

Congenital rubella case reporting is presumably better than that for postnatal rubella, but underreporting exists, due largely to misdiagnosis (especially of cases where defects are not discovered in the neonatal period) and lack of interest in reporting.[1] Could the 1979-1980 increase in reported cases of CRS in infants born in San Francisco Bay Area counties be an arti-

fact due to changes in diagnostic and reporting thoroughness?

The 1979 outbreak and attendant publicity undoubtedly generated concern, so that it is likely that more pregnant women reported either rash illness or exposure to persons with rash illness

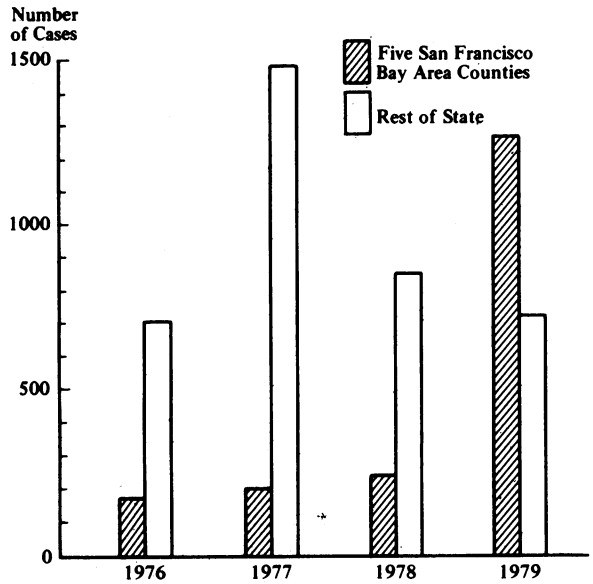

Figure 1.—Reported cases of rubella in California for the calendar years 1976 through 1979.

to their obstetricians, thereby promoting increased attention to the possibility of CRS in the infants subsequently delivered. The 1979-1980 increase in reports of infants with rubella infection only (without any apparent defects) suggests that this phenomenon occurred. Most of the 13 CRS cases in the San Francisco Bay Area had major CRS stigmata, which should have promoted efforts to obtain laboratory confirmation even in the absence of maternal rash illness or exposure histories (Table 1); however, 5 of these cases might have gone undiagnosed or unreported had not the medical staff at one referral medical center made a special effort to assure that suspected cases were studied for laboratory confirmation and reported if confirmed. Staff at this medical center are certain, nevertheless, that the 1979-1980 increase in CRS cases was a real one and not simply a reflection of heightened diagnostic attentiveness.

Poorer reporting of cases of CRS in infants born outside of the San Francisco Bay Area is suggested by Figure 2, in that for the first three years the number of reported CRS cases for the five San Francisco Bay Area counties nearly equals that for the rest of the state, even though these counties comprise only a fifth of the state's population. Three laboratories in Southern California, where over half of the state's population resides, carry

TABLE 1.—*Clinical and Laboratory Features of San Francisco Bay Area Infants With Congenital Rubella Syndrome, Born Between July 1979 and August 1980*

	Case Number												
	1	2	3	4	5	6	7	8	9	10	11	12	13*
Clinical and laboratory features													
Cataracts	..	x	x	x	x	x	x	x	..	..	..	x	..
Mental/developmental retardation	..	..	..	..	..	..	..	..	x	..	..	x	..
Hearing loss	..	x	..	..	x	x	..	..	..	..	..	..	..
Congenital heart disease													
Patent ductus	x	x	..	..	x	x	..	..	x	..	..	x	x
Pulmonic stenosis	..	..	..	..	..	..	x	x	x	..	..	..	..
Unspecified type	..	..	x	x	..	..	..	..	..	x	..	..	..
Meningoencephalitis	..	x	..	..	..	..	..	..	..	..	..	..	..
Microcephaly	..	..	..	..	..	..	..	..	..	..	..	x	x
Low platelet count and/or purpura	x	x	..	..	..	x	x	x	..	..	x	..	..
Enlarged spleen	..	x	..	..	x	..	x	x	..	..	x	..	..
Enlarged liver	..	x	..	..	x	..	x	x	x	..	x	..	..
Long bone radiolucencies	x	..	..	..	..	x	x	x	..	..	..	..	..
Congenital glaucoma	..	..	..	..	..	..	..	..	..	..	..	..	..
Jaundice (onset within 24 hours)	..	..	..	..	..	..	..	..	..	..	..	..	..
Pigmentary retinopathy	..	..	..	..	..	..	..	..	..	..	..	..	..
Laboratory confirmation													
Rubella virus isolated (from throat, N/P, urine, lens, etc.)	x	..	x	x	x	x	x	x	x	x	x	..	..
Rubella IgM antibody	..	x	..	..	..	x	..	..	..	x	..	..	..

N/P = nasopharyx

*Mother had history of rash illness in early pregnancy. Shortly after birth, serum rubella HI antibody titers for both the mother and infant were 1:512. (HI = hemagglutination inhibition)

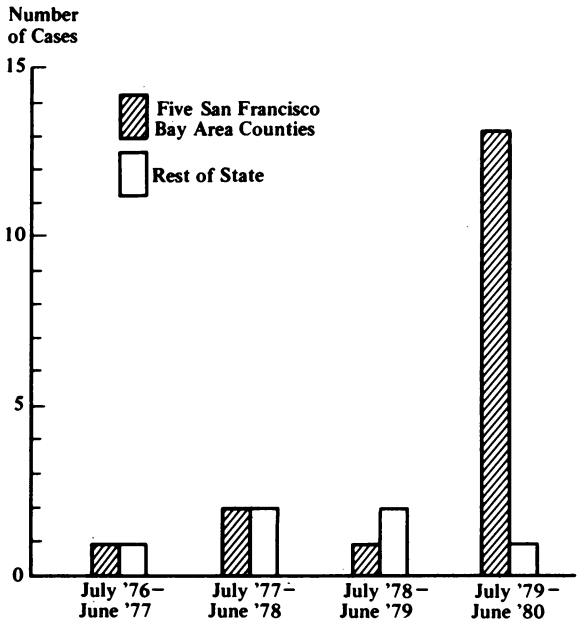

Figure 2.—Confirmed or probable cases of congenital rubella syndrome reported in California for the July-June years 1976-1977 through 1979-1980.

out rubella virus isolations. Records from these laboratories were not reviewed, and it may be that underascertainment of laboratory-confirmed cases was greater in Southern California. However, there is no reason to suspect that the degree of underascertainment changed during the time shown in Figure 2, and, thus, no evidence exists for a secular change in CRS incidence outside of the five San Francisco Bay Area counties.

Thus, while increased diagnostic and reporting thoroughness played some role, we strongly suspect that most of the observed 1979-1980 increase in San Francisco Bay Area cases of CRS is real and is a consequence of the 1979 outbreak. This episode should serve as a reminder that, despite the administration of more than 100 million doses of rubella vaccine in the United States during the past 11 years, rubella is still a relatively common disease in this country, capable of producing outbreaks followed by groups of CRS cases. As was the case in this episode, most recent rubella outbreaks have involved predominantly older teenagers and young adults—that is, the age group in which pregnancy is most common.[1] The economic impact of a CRS case is substantial. The average lifetime medical cost of such a child has been estimated to be $161,000 in 1975 dollars, a figure that does not include indirect costs that result from loss of productivity due to disability or premature death.[2]

While information on rubella immunization histories and reasons for lack of prior immunization was not obtained on the mothers of the infants with CRS associated with this outbreak, such information was secured for a similar outbreak that occurred in Chicago in 1978.[3] In the latter outbreak, investigation of mothers of 30 infants with CRS showed that none had been immunized. Two thirds of them were unmarried and, therefore, could not have been helped by premarital screening. Others were primiparas, and thus could not have been helped by previous prenatal screening and postpartum immunization. Moreover, it was found that only a small minority of seronegative women who had delivered babies in a Chicago area hospital that was surveyed had received rubella vaccine postpartum.

To prevent recurring cycles of rubella outbreaks and subsequent clusters of CRS cases, high priority must be given to the rubella immunization recommendations of the United States Public Health Service.[4]

First, essentially all girls and boys should be immunized against rubella at a young age (preferably, rubella vaccine is given in combination with measles and mumps vaccines at 15 months of age). To insure near-universal immunization and resultant "herd immunity," emphasis must be placed on rigorous enforcement of the laws, which are now in effect in virtually all 50 states, requiring rubella immunization for school entry.

Second, emphasis must also be placed on selective immunization of females of childbearing age who are known or suspected to be susceptible to rubella. These women must not be pregnant at the time the vaccine is administered and should understand that they should avoid pregnancy for three months after immunization. Suggested "checkpoints," that is, times when or where immunization can be given to women include the following: (1) when entering college or military service, (2) just before marriage, (3) immediately after childbirth and (4) while attending family planning clinics.

Clearly, however, there are problems in establishing programs to immunize postpubertal women. California has had a premarital rubella serological screening requirement since 1974, but a number of factors have hindered its effectiveness: (1) about 18 percent of live births in the state are to unmarried women, some of whom have never been married and, thus, have not been screened;

(2) "confidential" marriages and out-of-state marriages, both of which usually escape the screening requirement, now comprise almost 40 percent of marriages by Californians; (3) an unpublished survey conducted in 1976 by the DHS on a group of women identified as seronegative at premarital screening found that only a fourth of them had obtained rubella immunization two to three months after marriage, though another 60 percent stated that they intended to do so. Another survey found that many California women who had been screened serologically just before marriage were unaware of the result.[5] In Colorado and Rhode Island, premarital rubella screening requirements appear to have operated somewhat more effectively than in California, possibly because in these other programs, most of the testing is done in state laboratories and counseling of seronegative women on the need for immunization is built into the notification system.[6,7] With all programs to immunize postpubertal women there is the problem of inadvertent immunization just before or during early pregnancy; these episodes produce considerable anxiety and sometimes result in therapeutic abortions, though the teratogenicity risk associated with the vaccine is very small and possibly nil.[1]

Conclusion

In spite of the difficulties cited, we feel that the threat of rubella infection in early pregnancy remains sufficiently great that programs to identify and immunize females of childbearing age should be strengthened and pursued aggressively. Women discovered to be seronegative for rubella must be given concise, effective counseling on the nature of the threat of CRS and the need for rubella immunization at an appropriate time. These activities are particularly important at present, because several years must elapse before the herd immunity, resulting from implementation of recently enacted requirements for school-entry rubella immunization, can be expected to exert its full impact.

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